

REMARKS

I. Amendments to the Specification

The "Cross-Reference to Related Application" paragraph has been amended for purposes of clarification. Specifically, this paragraph has been amended in order to characterize the present application as a continuation of U.S. Application No. 09/609,461, rather than a divisional thereof. This change has been made because, as noted by the Office (see page 2, paragraph 1 of the present action), the claims pending herein were not previously presented, and subject to a restriction, in U.S. Application No. 09/609,461. The paragraph has further been amended in order to update the status of the other nonprovisional applications from which the present application claims priority.

Two additional paragraphs, both in the Summary, have also been amended for purposes of clarification. Specifically, these paragraphs have been amended to define Y as a residue capable of initiating free radical polymerization upon *UV initiated* cleavage of the Y-S bond, rather than *homolytic* cleavage thereof. The present invention is directed to a method of preparing a polymer brush or sensor comprising such a brush, as well as the brush and sensor themselves, which employs an iniferter polymerization initiator. As noted in the present application, iniferter polymerization may proceed by UV initiated cleavage (see, e.g., page 39, line 6 to page 40, line 3 and Example 18, page 90, line 29 to page 92, line 12). It is further noted in the present application that when a surface-bound iniferter polymerization process is employed, it is the bond between Y and sulfur which is cleaved, not the bond between Y and the linker, L, because it is this latter bond which ensures Y remains attached to the surface (see, e.g., page 39, line 6 to page 40, line 3).

II. Amendments to the Claims

In this Amendment B, claim 17 has been amended to amplify particular embodiments of the present invention. More specifically:

- The claim has been amended to insert the units for the molecular weight of the water-dispersible segment. Support for this amendment may be

found, for example, on page 14, lines 18-19, page 59, lines 23-24 and page 60, line 2.

- The claim has been amended to require that not all of the monomers in the monomer mixture are functionalized; that is, the claim requires that (i) either the acrylamide-based monomer or the at least 1 other monomer has one or more functionalized sites thereon for binding a probe, and (ii) at least one of said monomers does not have such functionalized sites. Support for this amendment may be found, for example, on page 47, lines 13-23.

Additionally, new claims 29-31 have been added. Support for claims 29 and 30 may be found in the application, for example, on page 47, lines 13-23. Support for claim 31 may be found, for example, in claim 17 prior to the amendment thereto.

III. Status of Pending Claims

Applicants acknowledge the cancellation of claims 1-16. However, with respect to claim 28, Applicants respectfully submit that the sensor of this claim is in fact not the same as the sensor of cancelled claim 8. As such, the previous Restriction requirement did not apply to claim 28 and, therefore, Applicants had no reason to submit a traversal related thereto.

More specifically, it is to be noted that canceled claim 8 was directed to a sensor made by a process which required, among other things, that the derivatized surface be contacted with a composition that comprised unbound iniferter initiator. Claim 17, from which claim 28 depends, does not. Furthermore, claim 17 requires that the water-dispersible segment of the polymer chains have a weight average molecular weight of at least about 1000 grams per mole. Canceled claim 8 had no such requirement.

Given the close relationship between claim 28 and claims 17-27, claim 28 being directed to the product of the processes of claims 17-27, Applicants respectfully submit a restriction between these claims would be improper. Specifically, Applicants respectfully submit that, even assuming *arguendo* claim 28 and claims 17-27 are

directed to independent and distinct inventions, as required by 35 U.S.C. §121, the Office is still required to examine these claims, per the MPEP §803 which states:

"[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent and distinct inventions."

Accordingly, Applicants respectfully submit claims 17-28, as well as new claims 29-31, are pending and should be under examination in the present application.

IV. 35 U.S.C. §112, First Paragraph (Enablement)

Reconsideration is respectfully request of the rejection of claims 17, 18 and 23-27 for containing subject matter which is not described in the specification in such as way as to enable one skilled in the art to make or use the invention commensurate in scope with these claims. This rejection is based on the assertion that the specification provides no enabling written description of the structural or chemical requirements of the moiety "L" which, according to the Office could include moieties as diverse as metal containing macrocycles and reactive acetylene linkages which would not be useful for the stated purpose of the invention.¹

A specification must be taken as in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for the enabling support. (See, e.g., *In re Marzocchi*, 439 F.2d 220, 223-4 (CCPA 1971); see also MPEP §2164.04). As a result, the burden rests on the Patent Office to establish a *prima facie* case of nonenablement, which requires the Office to provide acceptable evidence or

¹ It is to be noted that Applicants understand this rejection to be based on an asserted lack of enabling disclosure, given the multiple references thereto, rather than one of written description. However, should this rejection actually be based on lack of written description sufficient to show possession of the invention as claimed, Applicants respectfully request reconsideration, particularly in view of (i) the passages in the specification noted in the rejection as well as those noted herein, and (ii) the strong presumption which exists that adequate written description of the claimed invention is present when the subject claim language was in the claim *as originally filed*.

reasoning inconsistent with the contested statements. (*Id.*; see also *In re Strahilevitz*, 668 F.3d 1229, 1232.)

In this instance, Applicants respectfully submit the Office has failed to establish a *prima facie* case of nonenablement with respect to the invention as defined by claims 17, 18 and 23-27. Specifically, the Office has failed to provide acceptable evidence or reasoning to support its assertion that these claims contain subject matter which is not described in the specification in such a way as to enable one skilled in the art to make or use the invention commensurate in scope with these claims. Rather, the Office has merely noted some of the passages in the application which address the linking moiety, and then simply provided a conclusory statement that this was not enabling. Hence, the Office has failed to apply the standard for determining whether the specification meets the enablement requirement which, pursuant to MPEP §2164.01, effectively requires the Office to provide evidence or reasoning that the experimentation needed to practice the invention as claimed is undue or unreasonable. (See, e.g., *In re Wands*, 858 F.2d 731, 737.) As such, the Office does not set forth a *prima facie* basis of non-enablement.

Moreover, the specification provides substantial guidance to one of ordinary skill in the art in selecting a linking moiety, including for example:

- i. page 26, line 16 to page 27, line 20 provides a general discussion related to the optional status of the linker, when a linker may be used, the type of linker that may be used, and when a silicon atom may be beneficial to include in the linker;
- ii. page 66, lines 14-19 includes a passage related to alkyl groups, which is one of the forms the linker may take;
- iii. page 67, lines 10-18 includes a passage related to heteroalkyl and alkoxy groups, which are other forms the linker may take; and,
- iv. page 76, line 20 to page 77, line 7 (related to Examples 2-14) provides chemical structures of compounds that include an exemplary silicon-containing, alkoxy linking moiety.

Finally, with respect to the comment that the definition of the linking moiety in the present application may encompass linkages that would not be useful for the intended purpose of the invention, Applicants respectfully point out that it is not a function of the claims to specifically exclude possible inoperative embodiments. (See, e.g., *Atlas Powder*, 224 USPQ 409, 413 (Fed. Cir. 1984).)

In view of the forgoing, reconsideration of this rejection is respectfully requested.²

V. 35 U.S.C. §112, First Paragraph (Written Description)

Reconsideration is requested of the rejection of claims 17-27 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

A. *Monomer Combination*

Reconsideration is respectfully requested of the rejection of claim 17-27 based on the assertion that Preliminary Amendment A, filed February 28, 2003, added new matter to the claims that is not described in the specification as originally filed. The Office has asserted that there is no description in the specification of the specific monomer reagent combination recited in claim 17; that is, the Office asserts the specification fails to provide a description for a composition comprising a water-soluble or water-dispersible free radically polymerizable monomer mixture which contains an acrylamide-based monomer and at least 1 other monomer.

Applicants respectfully point out that the claim language at issue here was part of claim 17 as originally filed. Per MPEP §2163, II. A., in such instances, there is a strong presumption that an adequate written description of the claimed invention is present in

² In response to the comment that Example 18, under the heading "3-Synthesis of polymer brushes" (page 91), does not describe the addition of any monomer, Applicants respectfully call attention to lines 25-26, wherein it is clearly stated that each silicon wafer was immersed in distilled dimethylacrylamide (i.e., the monomer), prior to UV irradiation. Applicants did not address this comment above because it did not seem to be relevant to the present rejection.

the specification as filed. Furthermore, support for the above-noted claim language may be found in the specification, for example:

- i. on page 47, line 24 to page 48, line 24, wherein acrylamide monomers are identified as a particularly useful class of water-soluble or water-dispersible monomers; and,
- ii. on page 49, line 1 to page 50, line 12 (the paragraph which immediately follows the above-noted text), wherein it is stated that a copolymer may include two or more of the previously mentioned acrylamide-based repeat units, or it may include one of the previously mentioned acrylamide-based repeat units in combination with one or more other repeat units (i.e., at least one other monomer).

In view of this disclosure, Applicants respectfully submit that the Office cannot fairly maintain that the noted passage of claim 17 is not supported by the specification. Given that a strong presumption of compliance with the written description should be afforded to claim 17 in this instance, reconsideration of this rejection is respectfully requested.

In as much as claims 18-27 depend directly or indirectly from claim 17, reconsideration of the rejection of these claims is respectfully requested for the same reasons as set forth with respect to claim 17.

B. UV Initiated Cleavage

Reconsideration is respectfully requested of the rejection of claim 17-27 based on the assertion that there is no support in the specification for the definition in claim 17 of "Y" as a residue capable of initiating free radical polymerization upon *UV initiated* cleavage of the Y-S bond.

As to whether the written description requirement of 35 U.S.C. §112 has been met with respect to the use of the term *UV initiated* cleaving in claim 17, it should first be noted that the specification need not recite every detail associated with the preparation the claimed sensor. In fact, the MPEP states that the subject matter of the

claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement.³ Furthermore, according to the Federal Circuit, "[a]n objective standard for determining compliance with the written description requirement is 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed.'"⁴

Applicants respectfully submit that the present application supports claim 17, and furthermore unquestionably conveys to one of ordinary skill in the art that they had possession of the invention as claimed. More specifically, the specification, in relevant part, indicates the present application is directed to a method of preparing a sensor for detecting a biological molecule in an aqueous sample which employs an iniferter polymerization initiator (see, e.g., the Summary, prior to the amendment made herein, on page 6, lines 2-3). The specification also notes that the iniferter polymerization proceeds by UV initiation (see, e.g., page 39, line 6 to page 40, line 3 and Example 18, page 90, line 29 to page 92, line 12). Finally, the specification notes that when a surface-bound iniferter polymerization process is employed, it is the bond between Y and S (i.e., sulfur) which is cleaved, not the bond between Y and the linker, L, because it is this latter bond which ensures Y remains attached to the surface (see, e.g., page 39, line 6 to page 40, line 3).

In view of the foregoing, Applicants respectfully submit that the specification does in fact provide sufficient support for claim 17. Reconsideration of this rejection is therefore respectfully requested.

In as much as claims 18-27 depend directly or indirectly from claim 17, reconsideration of the rejection of these claims is respectfully requested for the same reasons as set forth with respect to claim 17.

VI. Provisional Obviousness-type Double Patenting Rejection

Claims 17-27 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over (a) claims

³ MPEP 2163.02.

⁴ In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989).

92, 102-104 and 107 of co-pending U.S. Patent Application No. 09/609,461 and (b) claims 85-91 and 94-101 of co-pending U.S. Patent Application No. 10/043,394. In response thereto, Applicants enclose with this Amendment B a Terminal Disclaimer in accordance with 37 C.F.R. 1.130(b) and 37 C.F.R. 1.321(c).

However, it is to be noted that this Disclaimer is being submitted in order expedite examination and allowance of the present application, particularly given that the term of this application will not be affected. Accordingly, Applicants make no representations as to whether or not this rejection is proper with respect to U.S. Patent Application No. 10/043,394 and expressly reserve the right to do so in that Application, should such a rejection be made therein at a later date.

In view of the foregoing, Applicants respectfully submit that the obviousness-type double patenting rejections have been obviated and, therefore, respectfully request these be withdrawn.

VII. 35 U.S.C. §102(a) Rejection

Reconsideration is respectfully requested of the rejection of claims 17 and 18 under 35 U.S.C. §102(a) as being anticipated by Nakayama et al. (Langmuir **1999**, 15, pp. 5560-66, hereinafter "Nakayama 126").

Claim 17, from which claim 18 depends, is directed to a method of preparing a sensor for detecting a biological molecule in an aqueous sample. This method comprises, *in relevant part*:

bonding an iniferter initiator to a substrate surface to form a derivatized surface;

contacting said derivatized surface with a composition comprising a water-soluble or water-dispersible free radically polymerizable **monomer mixture**, the mixture containing an acrylamide-based monomer and at least 1 other monomer, under reaction conditions to form bound polymer chains comprising a water-dispersible segment having a weight average molecular weight of at least about 1000 grams per

mole, wherein (i) at least one of said monomers has one or more functionalized sites thereon for reaction with a probe selective for the biological molecule, and (ii) **at least one of said monomers does not have a functionalized site for reaction with said probe**; and,
bonding the probe to the bound polymer chains through the functionalized sites.

Accordingly, claim 17 is directed to a method which comprises contacting the surface-bound iniferter initiator with a *monomer mixture*. Furthermore, claim 17 requires that the acrylamide-based monomer or one of the at least 1 other monomers is not functionalized; that is, the claim requires that, of the monomers present in the mixture, at least one is functionalized and at least one is not functionalized, for purposes of reaction with the probe that is selective for the biological molecule of interest.

In contrast to the requirements of claim 17, Nakayama 126 does not disclose a method wherein the derivatized surface of the substrate is exposed to a *monomer mixture*. Accordingly, this reference also does not disclose a mixture containing monomers that are functionalized for binding a probe and monomers which are not functionalized for binding a probe. Rather, in Nakayama 126, when more than one monomer is used, a *block* copolymerization method is employed, wherein the derivatized surface of a film is first exposed to one monomer in a polymerization reaction. After this first polymerization, the treated film is thoroughly rinsed and dried, to remove unreacted monomers and homopolymers. Finally, after this, the treated film is exposed to another monomer in another, separate polymerization reaction. (See, e.g., paragraph on page 5561-62 under the heading "Surface Block-Graft-Copolymerization.")

In view of the foregoing, it is to be noted that an element of claim 17 is lacking in the cited reference. Reconsideration of the rejection of claim 17 is therefore respectfully requested. Furthermore, in as much as claim 18 depends from claim 17, this claim is submitted as novel over the cited reference for the same reason as set forth with respect to claim 17.

VIII. 35 U.S.C. §103 Rejection

Reconsideration is respectfully requested of the rejection under 35 U.S.C. §103 of (i) claims 17-27 as being obvious in view of de Boer et al. in combination with Sundberg et al. (U.S. Patent No. 5,919,523), and (ii) claims 17, 18, 24 and 25 as being obvious in view of Nakayama (Macromolecules **1996**, 29, pp. 8622-8630, hereinafter "Nakayama 125") in combination with Sundberg et al.

Claim 17, from which claims 18-27 depend, is directed to a method of preparing a sensor for detecting a biological molecule in an aqueous sample. This method comprises, *in relevant part*:

bonding an **iniferter initiator** to a substrate surface to form a derivatized surface;

contacting said derivatized surface with a composition comprising a water-soluble or water-dispersible free radically polymerizable **monomer mixture**, the mixture containing an acrylamide-based monomer and at least 1 other monomer, under reaction conditions to form bound polymer chains comprising a water-dispersible segment having a weight average molecular weight of at least about 1000 grams per mole, wherein (i) at least one of said monomers has one or more functionalized sites thereon for reaction with a probe selective for the biological molecule, and (ii) **at least one of said monomers does not have a functionalized site for reaction with said probe**; and,

bonding the probe to the bound polymer chains through the functionalized sites.

Accordingly, claim 17 is directed to a method which employs a *living* or a *living-like* polymerization process, in that an iniferter initiator is used.⁵ As noted in the present

⁵ It is well-recognized that using an iniferter initiator in a polymerization reaction is one way to perform a polymerization under living or living-like reaction kinetics. (See, for example, the cited references by Nakayama and de Boer for evidence that iniferter initiated polymerization reactions are living or living-like.)

application, a living polymerization is preferred because it enables greater control of polymer molecular weight and polydispersity. (See, e.g., page 21, line 22 to page 22, line 20.)

Furthermore, claim 17 requires that the surface-bound iniferter initiator be contacted with a monomer mixture, wherein the acrylamide-based monomer or one of the at least 1 other monomers in this mixture is not functionalized; that is, claim 17 requires that, of the monomers present in the mixture, at least one is functionalized and at least one is not functionalized, for purposes of reacting with the probe that is selective for the biological molecule of interest. As noted in the present application, such a monomer mixture is beneficial because it enables the number of functional groups in the surface-bound polymers chains to be controlled, which in turn enables greater control of functional group accessibility for the probe that is to be attached. (See, e.g., page 47, lines 13-23 and page 10, line 25 to page 11, line 9.)

In contrast to the invention of claim 17, both de Boer and Nakayama 125 fail to disclose or suggest a method wherein the iniferter-derivatized surface of the substrate is exposed to a *monomer mixture*. Accordingly, these references also fail to disclose or suggest a mixture containing monomers that are functionalized for binding a probe and monomers which are not functionalized for binding a probe. Rather, in both de Boer and Nakayama 125, when more than one monomer is used, a *block* copolymerization method is employed, wherein the iniferter-derivatized surface is first exposed to one monomer in a polymerization reaction and, after than reaction is complete, the resulting surface is exposed to a second monomer.⁶ Furthermore, the monomers employed by de Boer (i.e., styrene and methyl methacrylate) are not water-soluble or water-dispersible, as is also required by claim 17.

Sundberg et al. also fail to disclose or suggest the method of claim 17, both alone and in combination with de Boer or Nakayama 125. More specifically, Sundberg et al. fail to disclose or suggest a method wherein an *iniferter*-derivatized surface is prepared. Furthermore, they also fail to disclose or suggest contacting the derivatized

⁶ (See, for example, the paragraph extending from page 850 to page 851 in de Boer under the heading "Living Free Radical Photopolymerization," and the paragraph on page 8627 in Nakayama 125 under the heading "Surface Block Graft Copolymerization.")

surface with a mixture containing monomers that are functionalized for binding a probe and monomers which are not functionalized for binding a probe. In fact, to the extent that Sundberg et al. are concerned with functional site density, their focus is on that of the substrate surface, rather than the polymer chains attached thereto. (See, e.g., col. 11, lines 5-10.)

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. And third, the prior art reference must teach or suggest all the claim limitations. MPEP §2142. With all due respect, the Office has failed to establish a *prima facie* case of obviousness, because motivation is clearly lacking to combine the cited references. More specifically, while Nakayama 125 and de Boer are directed to living or living-like polymerization processes which utilize an iniferter initiator, Sundberg et al. clearly is not. In fact, Sundberg et al. fail to even reference such a polymerization process. Accordingly, it is only through impermissible hindsight, in view of the present application, that one of ordinary skill in the art would be led to utilize the monomer mixtures of Sundberg et al. in the processes disclosed by Nakayama 125 or de Boer.

Furthermore, even assuming *arguendo* such a combination of references were permissible, the prior art references cited by the Office individually and collectively fail to disclose or suggest each of the requirements of claim 17. In particular, none of the cited references disclose or suggest a method for preparing a sensor for detecting a biological molecule which comprises applying a mixture of monomers, some of which have functional groups for binding a probe and some of which do not, a feature which advantageously enables the functional site density on the resulting polymers to be controlled.

In view of the foregoing, it is respectfully submitted that the rejection of claim 17 under 35 U.S.C. §103, as being unpatentable over de Boer et al., or Nakayama 125, in view of Sundberg et al., is improper and thus should be withdrawn.

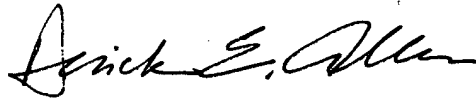
Claims 18-27, as well as new claims 29-31, depend directly or indirectly from claim 17 and are, therefore, respectfully submitted as patentable over the cited

combination of references for the same reasons as those set forth with respect to claim 17, and further in view of the additional requirements which they introduce. In the interest of brevity, however, each of these additional requirements will not be argued at this time.

CONCLUSION

* Enclosed is a check for \$1060.00, for a three (3) month extension of time and the required Terminal Disclaimer Fee. The Commissioner is hereby authorized to charge any underpayment or credit any overpayment to Deposit Account No. 19-1345.

Respectfully submitted,



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*Enclosures

DEA/skd